

Applicants: Ron S. Israeli, et al.
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Rejection under 35 U.S.C. 112, first paragraph

The Examiner rejected claims 97-100 and 103 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner stated that pages 52-53 of the specification disclose that SEQ ID NO:2 can be found in normal prostate cells, benign hyperplasia, and in a transformed prostate cell line, in addition to prostate cancer cells. The Examiner stated therefore, the skilled artisan would have to perform undue experimentation without a reasonable expectation of success because the instant invention while marking prostate cells, does not mark prostate cancer cells and cannot differentiate them from normal prostate cells, and therefore cannot be used in a method to detect micrometastatic prostate tumor cells.

In response, applicants respectfully traverse the Examiner's above rejection. Although prostate specific membrane antigen may be expressed on both normal and malignant prostate epithelial cells, its expression is significantly enhanced on malignant cells. In support, applicants attach hereto as **Exhibit A** a copy of Wright et al. (1995) entitled "Expression of Prostate-Specific Membrane Antigen in Normal, Benign, and Malignant Prostate Tissues" Urol. Oncol 1:18-28. On page 27, in column 1 Wright et al. state that this "study demonstrates the **differential expression** of PSMA in normal, benign and malignant prostate tissues" [emphasis added]. The paper also states that "PSMA was **overexpressed** in the poorly differentiated and metastatic tumors" [emphasis added]. In further support of this fact, applicants attach hereto as **Exhibit B** a copy of Sweat et al. (1998) entitled "Prostate-Specific Membrane Antigen Expression is Greatest in Prostate Adenocarcinoma and Lymph Node Metastes" Urology 52(4):637-640. On page 640, in column 1 Sweat et

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al. state "we found consistent PSMA immunoreactivity in benign epithelium, primary prostate cancer, and lymph node metastases, with expression highest in cancer and lymph node metastases." These papers establish that there is differential expression of PSMA in normal and cancer cells. Since there is a differential expression of PSMA between normal and cancer cells, then one skilled in the art would be able to compare the amount of PSMA mRNA measured in a sample obtained from subject with an amount measured in a control sample, wherein a higher amount of PSMA mRNA would be expected if the sample was cancerous since PSMA is overexpressed in cancer cells. Therefore, the claimed invention is enabled because one skilled in the art would be able to detect micrometastatic prostate tumor cells by identifying an elevated amount of PSMA mRNA using the claimed method without undue experimentation and with a reasonable certainty of success. Applicants contend that these remarks and amendments obviate the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. 112, second paragraph

The Examiner rejected claim 98 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner stated that clause (e) repeats the word detect twice.

In response, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove amended claim 98 such that it no longer recites the word "detect" twice. Applicanst contend that this amendment obviates the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

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U.S. Serial No. 08/242,404

Pursuant to their duty of disclosure under 37 C.F.R. §1.56, applicants disclose the existence U.S. Serial No. 08/242,404, filed May 13, 1994, which is a divisional of U.S. Serial No. 07/668,569, filed March 13, 1991, and is licensed to Cytogen Corp, which is also the licensee of the subject application and whose counsel had informed the undersigned of its existence on November 20, 2000.

Claims 100-102

Applicants hereby acknowledge the Examiner's statement that claims 100-102 are in condition for allowance.

Summary

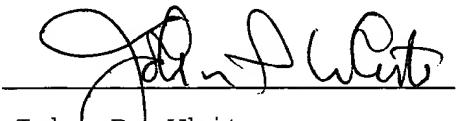
For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of objection and rejection and earnestly solicit allowance of the now pending claims.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

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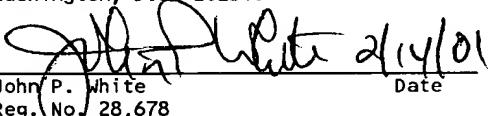
No fee, other than the enclosed \$445.00 fee for a three-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.


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Date